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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/667,283	09/17/2003	Thomas A. Dobbins	632898-041	8633

27805 7590 12/12/2007

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EXAMINER	
ROBERTS, LEZAH	
ART UNIT	**PAPER NUMBER**
1614	
MAIL DATE	**DELIVERY MODE**
12/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/667,283	DOBBINS ET AL.	
	Examiner	Art Unit	
	Lezah W. Roberts	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *7-11,21-25 and 34-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,12-20,26-33 and 37-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the Amendment filed November 20, 2006. All previous rejections have been withdrawn unless stated below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims

Claim Rejections - 35 USC § 102 – Anticipation (New Rejection)

Claims 29-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Nissen (US 6,103,764).

Nissen discloses administering salts of hydroxy beta methylbutyric (HMB) acid to animals for increasing the aerobic capacity of muscles of an animal and increases lean tissue development. The salts include calcium and magnesium salts. The compositions may be administered intravenously. The compounds are dissolved in a saline solution (col. 4, lines 5-10). The reference anticipates the instant claims insofar as it discloses a composition comprising and alkaline earth metal component, a biocompatible organic acid component and a normal saline solution.

Claim Rejections - 35 USC § 103 – Obviousness (New Rejection)

1) Claims 1-6, 12-20 and 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nissen (WO 94/17678) in view of Register (US 6,322,821) and Carnes et al. (US 4,185,093).

Nissen discloses a method of providing increase nutritional value of colostrum and first milk of pregnant mammals using beta hydroxy beta-methylbutyric (HMB) acid or its calcium salt. HMB was previously reported to enhance immune response and also increase selectively the development of lean tissue. Calcium HMB (Ca-HMB) is the preferred form of administering HMB. Sodium, potassium and magnesium salts of HMB may also be used. Ca-HMB was administered in an effective amount of 0.5 to 100 mg per kg of body weight per 24 hours (page 8, paragraph 2). In regards to claim 20, if the amounts disclosed above were divided by 24 hours, the amounts administered every hour are encompassed by the instant claim. The reference differs from the instant claims insofar as it does not disclose the Ca-HMB is used to raise serum levels of calcium in the blood.

Register discloses veterinary compositions for treating milk fever in freshening cows and a method of administering the composition. The first milk or colostrum of a fresh cow has a high level of calcium and antibodies to benefit the newborn calf's immune system. The calcium found in the colostrum is taken from the bloodstream, thus lowering the serum calcium level of the cow and is replaced either by intestinal calcium absorption or by bone calcium resorption. Low serum calcium levels in the blood of freshening cows can cause hypocalcemia, commonly referred to as milk fever (col. 1, lines 30-50). The compositions comprise calcium to replace calcium and also other components to help calcium absorption. One component used is magnesium. Magnesium chloride provides the minerals magnesium, which replaces minerals used to make colostrum and also helps the cow absorb calcium (col. 5, lines 1-16). The

reference differs from the instant claims insofar as it does not disclose administering a calcium salt of hydroxy beta methylbutyric to replenish the calcium and a parenteral composition.

Carnes discloses treatments of hypocalcemia and cow syndrome, which are commonly known as milk fever, in animals. The reference is used to disclose different methods of administration when treating hypocalcemia. Traditional treatment has consisted of the administration of calcium salts intravenously, subcutaneously or intramuscularly. Examples of these treatments are calcium salts such as calcium chloride, calcium gluconate, calcium borogluconate, calcium hypophosphite, calcium lactate, calcium glycerophosphate and calcium levulinate used either alone or in combination or with salts of magnesium, potassium, phosphites and glucose. Examples of preparations previously tried are given in U.S. Pat. Nos. 2,140,291 and 3,553,148, which discloses a mixture of calcium compounds and magnesium salts. Calcium chloride, while providing a rapid response in the patient animals, has potential for toxicity and acute heart block if administered too rapidly or in too concentrated a solution (col. 1, lines 24-40). The reference differs from the instant claims insofar as it does not disclose the calcium salt is calcium hydroxymethyl butyrate.

Calcium hydroxymethyl butyrate is used to increase the nutritional value of colostrum, which, as disclosed by Register, comprises calcium that is taken from the blood thereby causing a decrease in calcium levels which may lead to hypocalcemia and magnesium. Therefore it would have been obvious to one of ordinary skill in the art to have treated hypocalcemia while increasing the nutritional value of the colostrum with

the calcium or magnesium hydroxymethyl butyrate of Nissen motivated by the desire to use a compound or mixture of compounds that not only raises the nutritional value of the colostrum but also replenishes or raises the calcium and magnesium levels in the system of the animal by introducing calcium and magnesium salts as well as enhance calcium absorption with the magnesium salt, as disclosed by the Register.

It would have been obvious to one of ordinary skill in the art to have formulated a parenteral formulation of calcium hydroxymethyl butyrate for administration to an animal to treat the conditions of the primary and secondary references motivated by the desire to use a traditional method of administering a compound for treating calcium deficiency, as disclosed by Carnes.

In regards to the amounts of each compound used and the ratio, normally, changes in result effective variables are not patentable where the difference involved is one of degree, not of kind; experimentation to find workable conditions generally involves the application of no more than routine skill in the art. In re Aller 105 USPQ 233, 235 (CCPA 1955). It would have been obvious to one of ordinary skill in the art to have found effective dosages for treating the conditions with calcium HMB or a mixture of calcium HMB and magnesium HMB motivated by the desire to obtain optimal efficacy for treating the conditions, as supported by case law.

2) Claims 1-6, 12-20, 27, 28, 32, 33 and 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nissen (6,103,764) in view of Klesges (US 5,942,255) and Fleming et al. (US 5,922,765).

Nissen discloses administering salts of hydroxy beta methylbutyric (HMB) acid to animals for increasing the aerobic capacity of muscles of an animal and increasing lean tissue development. The salts include calcium and magnesium salts and may be administered intravenously (col. 3, lines 41-45). Suitable doses of HMB with respect to the dose of the calcium salt of HMB to administer, as a function of the body weight of the animal, it is preferable to administer at least about 0.05 mg of the calcium salt of HMB per kg of body weight per 24 hours, more preferably, at least about 0.5 mg/kg body weight/24 hours, even more preferably, at least about 15 mg/kg body weight/24 hours, and most preferably, at least about 35 mg/kg body weight/24 hours. Under most circumstances, it will usually not be necessary to administer more than 100 mg/ kg body weight/ 24 hours, although higher amounts may be necessary and certainly can be used. Furthermore, the dose of HMB can be administered with any suitable frequency (e.g., one 6 g dose per day or two 3 g doses per day) and over any suitable time period (e.g., a single dose can be administered over a 5 minute time period or over a 1 hour time period) (col. 3). The reference differs from the instant claims insofar as it does not disclose calcium HMB increases blood serum levels of calcium.

Klesges is used as a general teaching to disclose the connection of aerobic capacity with calcium. When an individual exceeds their aerobic capacity as a result of the high intensity of their physical activity (by definition, a higher intensity than aerobic activity), that individual has entered a metabolic state where the oxygen supply to that individual's cells is inadequate and the cell is at least partially metabolically anaerobic. Those individuals that are physically active to the extent that they have exceeded their

aerobic capacity and are partially anaerobic may also be losing calcium to a greater extent that their calcium intake, or their calcium intake is inadequate, and those individuals are losing bone mineral content and/or losing lean tissue mass and /or not accumulating lean tissue mass to the extent they would if their calcium levels were adequate. Where an individual is losing calcium as a result of their physical activity, such as through perspiration, the administration of calcium is believed to help maintain an acceptable level of calcium in the blood, thereby obviating the need for calcium resorption from bone, and thereby preventing muscle weakness and, in fact, strengthening muscles (col. 5, line 63 to col. 6, line 20). The reference differs from the instant claims insofar as it does not disclose using the calcium salt of hydroxy beta methylbutyric to replenish the calcium lost by physical activity.

Fleming et al. disclose administering magnesium to treat exercise-induced muscle cramps, stiffness, pain or spasms caused by or related to production of oxygen free radicals. These are symptoms of hypomagnesemia. The neuromuscular effects of hypomagnesemia occur commonly in association with hypocalcemia (col. 1, lines 13-47). The reference differs from the instant claims insofar as it does not disclose using the calcium salt or magnesium salt of hydroxy beta methylbutyric to increase calcium and magnesium in blood serum.

The compositions of Nissen are treating conditions that result from low levels of calcium by increasing aerobic capacity thereby inhibiting the loss of calcium resulting physical activity. When the calcium salt is used, the calcium levels are being elevated and therefore replenishing calcium that has been lost due to physical activity. Therefore,

it would have been obvious to one of ordinary skill in the art to have treated conditions such as hypocalcemia by increasing the level of calcium in the blood with the calcium salt of HMB in Nissen motivated by the desire to not only increase the aerobic capacity to inhibit the removal of calcium from the blood but to also replenish the calcium that may have been lost during the process, as disclosed by Klesges.

It would also have been obvious to one of ordinary skill in the art to have used magnesium salt of HMB with the calcium salt of HMB disclosed by Nissen motivated by the desire to treat hypomagnesemia, which is commonly associated with hypocalcemia, as disclosed by Fleming et al.

In regards to the amounts of each compound used and the ratio, normally, changes in result effective variables are not patentable where the difference involved is one of degree, not of kind; experimentation to find workable conditions generally involves the application of no more than routine skill in the art. In re Aller 105 USPQ 233, 235 (CCPA 1955). It would have been obvious to one of ordinary skill in the art to have found effective dosages for treating the conditions with calcium HMB or a mixture of calcium HMB and magnesium HMB motivated by the desire to obtain optimal efficacy for treating the conditions, as supported by case law.

Obvious-Type Double Patenting- (Previous Rejection)

Claims 1-6, 12-20, 26-33 and 37-39 are provisionally rejected on the ground of obvious nonstatutory double patenting over claims 1-6 and 9-24 of copending

Application No. 10/797946. This is a provisional double patenting rejection since the conflicting claims have not yet been patented. The rejection is maintained.

Applicant argues parenteral administration are not obvious over the claims of the '946 application which relate to oral administration.

As previously stated in the prior Office Action dated June 15, 2006, although the '075 reference claims the oral administration of Ca-HMG, one of ordinary skill in the art would have found oral administration obvious over parenteral administration and visa versa since the '000 reference for example teaches that the different administrable pharmaceutically acceptable forms include, but are not limited to, solids, such as tablets or capsules, and liquids, such as intravenous solutions.

Claims 1-6, 12-20, 26-33 and 37-39 are rejected.

Claims 7-11, 21-25 and 34-36 are withdrawn.

No claims allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lezah W. Roberts whose telephone number is 571-272-1071. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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